STIC Search Report
EIC 1700

STIC Database Tracking Number: 213590

TO:	From:
Satya Gudibande Location: Rem 3a20 / 3c18 Art Unit : 1654 January 23, 2007 Phone: 571-272-8146 Serial Number: 10 / 520791	Jan Delaval Location: EIC 1700 Remsen 4a30 Phone: 571-272-2504 jan.delaval@uspto.gov

Search Notes

```
=> d his

     (FILE 'HOME' ENTERED AT 15:55:17 ON 23 JAN 2007)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:55:34 ON 23 JAN 2007
               E TUBULYSIN
L1           48 S E3
L2           14 S L1 AND NR>=1
               ACT SATYA520/A
              ---------
L3             STR
L4           16 SEA FILE=REGISTRY SSS FUL L3
              ---------
L5           21 S L2,L4
L6            5 S L5 NOT L4
L7             STR
L8            0 S L7
L9             STR L7
L10           0 S L9
L11            STR L9
L12           0 S L11

=> d sta que l12
L11             STR
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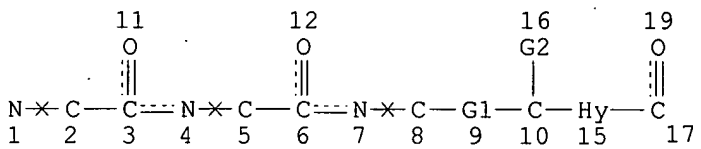


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VAR G2=O/S/N
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NSPEC   IS RC     AT   2
NSPEC   IS RC     AT   3
NSPEC   IS RC     AT   4
NSPEC   IS RC     AT   5
NSPEC   IS RC     AT   6
NSPEC   IS RC     AT   7
NSPEC   IS RC     AT   8
NSPEC   IS RC     AT  17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L12           0 SEA FILE=REGISTRY SSS SAM L11

  2.9% PROCESSED    2000 ITERATIONS                          0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:      1374843 TO 1406237
PROJECTED ANSWERS:               0 TO       0
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=> d sta que l8
L7                STR
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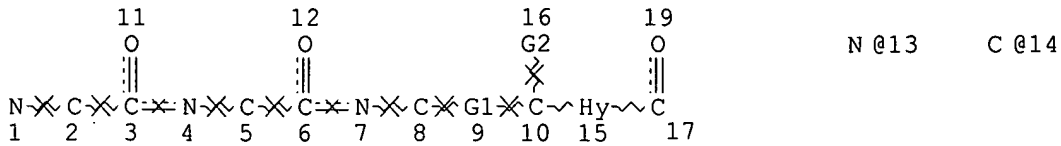


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VAR G2=O/S/N
NODE ATTRIBUTES:
NSPEC    IS RC     AT   1
NSPEC    IS RC     AT   2
NSPEC    IS RC     AT   3
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE
L8            0 SEA FILE=REGISTRY SSS SAM L7

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INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:      1944052 TO  1981228
PROJECTED ANSWERS:               0 TO        0
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=> fil reg
FILE 'REGISTRY' ENTERED AT 15:49:36 ON 23 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   22 JAN 2007  HIGHEST RN 918106-10-2
DICTIONARY FILE UPDATES:  22 JAN 2007  HIGHEST RN 918106-10-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

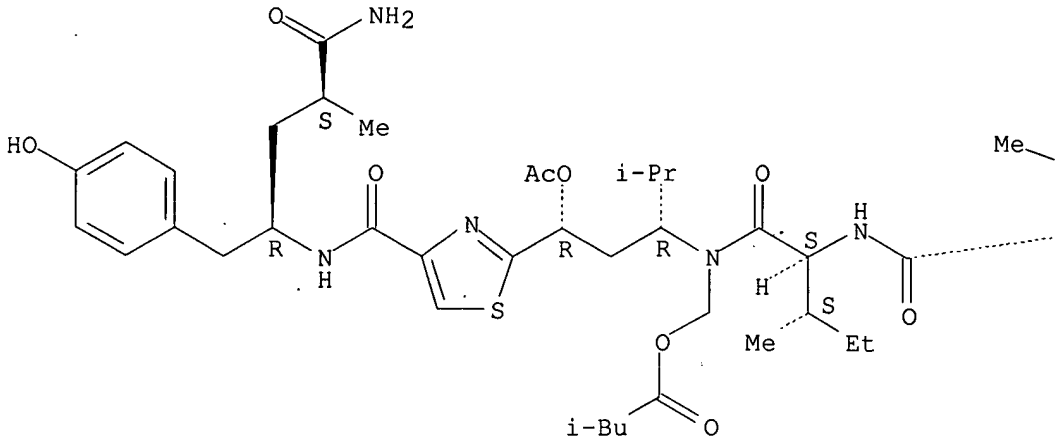
http://www.cas.org/ONLINE/UG/regprops.html

=> d ide can tot l15

L15  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   874108-55-1  REGISTRY
ED   Entered STN:  13 Feb 2006
CN   Butanoic acid, 3-methyl-, [[(1R,3R)-3-(acetyloxy)-3-[4-[[[(1R,3S)-4-amino-
     1-[(4-hydroxyphenyl)methyl]-3-methyl-4-oxobutyl]amino]carbonyl]-2-
     thiazolyl]-1-(1-methylethyl)propyl][(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-
     piperidinyl]carbonyl]amino]-1-oxopentyl]amino]methyl ester (9CI)  (CA
     INDEX NAME)
FS   STEREOSEARCH
MF   C43 H66 N6 O9 S
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
```

PAGE 1-A



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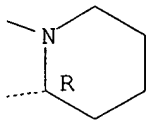


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

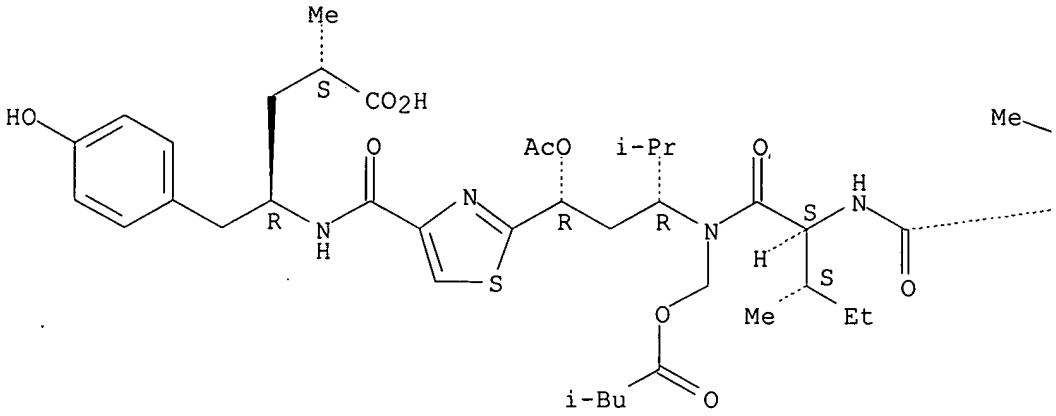
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:143058

L15 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN
RN **205304-86-5** REGISTRY
ED Entered STN: 10 May 1998
CN Benzenepentanoic acid, γ-[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-α-methyl-, (αS,γR)-(9CI) (CA INDEX NAME)
OTHER NAMES:
CN Tubulysin A
FS STEREOSEARCH
MF **C43 H65 N5 O10 S**
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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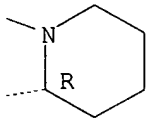


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

14 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 145:26562

REFERENCE 2: 145:508

REFERENCE 3: 144:460476

REFERENCE 4: 144:343554

REFERENCE 5: 144:187658

REFERENCE 6: 144:143058

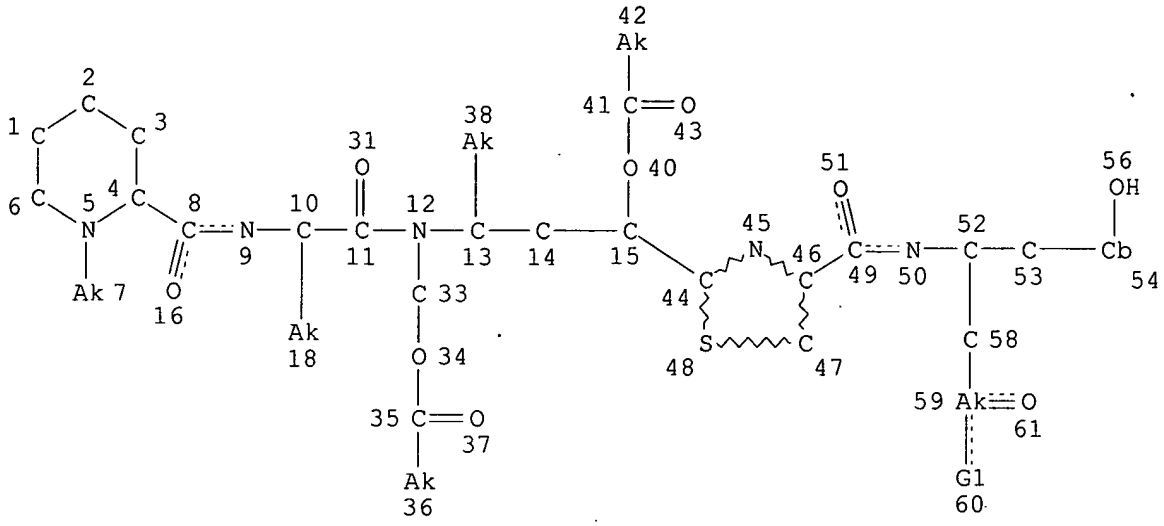
REFERENCE 7: 142:384897

REFERENCE 8: 142:19680

REFERENCE 9: 141:23346

REFERENCE 10: 140:248261

=> d sta que l23
L21 STR



VAR G1=O/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 44

STEREO ATTRIBUTES: NONE
L23 16 SEA FILE=REGISTRY SSS FUL L21

100.0% PROCESSED 72 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 15:22:53 ON 23 JAN 2007)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 15:23:05 ON 23 JAN 2007
L1 1 S US20050249740/PN OR (US2005-520791# OR WO2003-EP7415 OR DE200
E DOMLING/AU
L2 28 S E4,E5
E DOEMLING/AU
L3 43 S E4-E6
E WEBER/AU
L4 18 S E3
E WEBER L/AU
L5 318 S E3-E15
E WEBER LUTZ/AU
L6 205 S E3-E9
E MORPHOCHEM/PA,CS

```
L7          117 S E3-E58
L8           33 S (MORPHO?(L)KOMB?(L)CHEM?)/PA,CS
L9          117 S L7,L8
L10           7 S L1-L9 AND TUBULYSIN?
                SEL RN

     FILE 'REGISTRY' ENTERED AT 15:25:56 ON 23 JAN 2007
L11         118 S E1-E118
L12          19 S L11 AND NC5/ES AND 46.150.18/RID AND NCSC2/ES
L13           1 S L12 AND C43H66N6O9S
L14           1 S L12 AND C43H65N5O10S
L15           2 S L13,L14
L16        7934 S (16.299.11 AND 46.150.18 AND 46.156.1)/RID
L17           0 S L16 AND C2H4O
L18        1493 S L16 AND 3/NR
L19             STR
L20           0 S L19
L21             STR L19
L22           0 S L21
L23          16 S L21 FUL
                SAV L23 SATYA520/A
L24           0 S L23 AND C2H4O
L25          14 S L23 NOT L15
L26           1 S PEG/CN

     FILE 'HCAPLUS' ENTERED AT 15:46:46 ON 23 JAN 2007
L27          14 S L15
L28           1 S L26 AND L27
L29           1 S L1-L10 AND L28
L30           7 S L25
L31           0 S L30 AND L26
L32           2 S L27 AND POLYOXYALKYLENE?/CW,CT
L33           0 S L27 AND (PEG OR POLYETHYLENEGLYCOL OR POLYETHYLENEOXIDE OR PO
L34           1 S L27 AND (POLYETHYLENE GLYCOL OR POLY()(ETHYLENEGLYCOL OR ETHY
L35           0 S L27 AND (POLYETHYLENE OXIDE OR POLY()(ETHYLENEOXIDE OR ETHYLE
L36           0 S L27 AND (POLYOXY ETHYLENE OR POLY()(OXYETHYLENE OR OXY ETHYLE
L37           0 S L27 AND (POE OR PEO OR EO OR OE)
L38           2 S L28,L28,L32,L34

     FILE 'REGISTRY' ENTERED AT 15:49:36 ON 23 JAN 2007

=> d 126 ide can

L26  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   25322-68-3  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   α,ω-Hydroxypoly(ethylene oxide)
CN   α-Hydro-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN   α-Hydro-ω-hydroxypoly(oxyethylene)
CN   1,2-Ethanediol, homopolymer
CN   1660O
CN   1660S
CN   400DAB8
CN   636: PN: WO2006062685 SEQID: 669 claimed sequence
CN   Alkox
CN   Alkox E 100
CN   Alkox E 130
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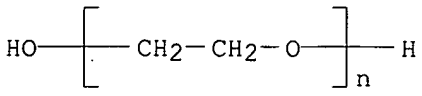
CN Alkox E 160
CN Alkox E 240
CN Alkox E 30
CN Alkox E 30G
CN Alkox E 45
CN Alkox E 60
CN Alkox E 75
CN Alkox LE
CN Alkox R 100
CN Alkox R 1000
CN Alkox R 15
CN Alkox R 150
CN Alkox R 400
CN Alkox SR
CN Alkox SW
CN Antarox E 4000
CN Aqua Calk TWB-P
CN Aquacide III
CN Aquaffin
CN Badimol
CN BDH 301
CN Bradsyn PEG
CN Breox 2000
CN Breox 20M
CN Breox 4000
CN Breox 550
CN Breox PEG 300
CN CAFO 154
CN Carbowax
CN Carbowax 100
CN Carbowax 1000
CN Carbowax 1350
CN Carbowax 14000
CN Carbowax 1450
CN Carbowax 1500
CN Carbowax 1540
CN Carbowax 20
CN Carbowax 200
CN Carbowax 20000
CN **PEG**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 6790-09-6, 9002-90-8
DR 615575-04-7, 876655-84-4, 12676-74-3, 12770-93-3, 9081-95-2, 9085-02-3, 9085-03-4, 174460-08-3, 174460-09-4, 54510-95-1, 125223-68-9, 54847-64-2, 59763-40-5, 64441-68-5, 64640-28-4, 133573-31-6, 25104-58-9, 25609-81-8, 134919-43-0, 101677-86-5, 99264-61-6, 106186-24-7, 112895-21-3, 114323-93-2, 50809-04-6, 50809-59-1, 119219-06-6, 60894-12-4, 61840-14-0, 37361-15-2, 112384-37-9, 67411-64-7, 70926-57-7, 75285-02-8, 75285-03-9, 77986-38-0, 150872-82-5, 154394-38-4, 79964-26-4, 80341-53-3, 85399-22-0, 85945-29-5, 90597-70-9, 88077-80-9, 88747-22-2, 34802-42-1, 107502-63-6, 107529-96-4, 116549-90-7, 156948-19-5, 169046-53-1, 188364-77-4, 188924-03-0, 189154-62-9, 191743-71-2, 196696-84-1, 201163-43-1, 206357-86-0, 221638-71-7, 225502-44-3, 270910-26-4, 307928-07-0, 356055-70-4, 391229-98-4, 402483-26-5
MF (C2 H4 O)n H2 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST,

CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

95320 REFERENCES IN FILE CA (1907 TO DATE)
24688 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
95672 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 146:92198

REFERENCE 2: 146:92188

REFERENCE 3: 146:92176

REFERENCE 4: 146:91344

REFERENCE 5: 146:91263

REFERENCE 6: 146:91213

REFERENCE 7: 146:90360

REFERENCE 8: 146:90138

REFERENCE 9: 146:89004

REFERENCE 10: 146:89002

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:50:00 ON 23 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 23 Jan 2007 VOL 146 ISS 5

FILE LAST UPDATED: 22 Jan 2007 (20070122/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitind hitstr retable tot 138

L38 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:515876 HCAPLUS
DN 145:26562
TI Muteins of human neutrophil gelatinase-associated lipocalin with affinity for cytotoxic T lymphocyte-associated antigen (CTLA-4) and their use for treatment of cancer, infectious, or (auto)immune diseases
IN Matschiner, Gabriele; Hohlbaum, Andreas; Schlehuber, Steffen; Poehlchen, Martin; Skerra, Arne
PA Pieris Proteolab A.-G., Germany
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006056464	A2	20060601	WO 2005-EP12640	20051125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI	US 2004-631200P	P	20041126
	US 2004-631202P	P	20041126
	US 2004-631227P	P	20041126
	US 2004-631253P	P	20041126
	US 2004-522970P	P	20041129
	US 2005-679811P	P	20050511
	US 2005-680067P	P	20050511

OS MARPAT 145:26562
AB The present invention relates to compds. with affinity for the cytotoxic T lymphocyte associated antigen (CTLA-4), wherein the compound exhibits a synergistic mode of action in that the the compound (a) increases T cell priming or T cell expansion or the generation of memory T cells by blocking of CTLA-4, and (b) enhances effector T cell activity in tumor tissue or lymphoid tissue by blocking of CTLA-4. The compound of the invention can be a protein, a small organic mol., a peptide, or a nucleic acid. The invention also relates to muteins derived from a protein selected from the group consisting of human neutrophil gelatinase-associated lipocalin (hNGAL), rat α2-microglobulin-related protein (A2m) and mouse 24p3/uterocalin (24p3). The muteins have binding specificity for CTLA-4, wherein said mutein: (a) comprises amino acid replacements at at least one of the sequence position corresponding to sequence positions

33-54, 66-83, 94-106, and 123-136 of hNGAL, and (b) binds human CTLA-4 with a KD of 50 nM or less. The serum half-life and pharmacokinetics of hNGAL muteins are improved by fusions with albumin-binding domains and/or by cysteine residue mutants. The invention also relates to a pharmaceutical composition comprising such a compound or mutein as well as to various pharmaceutical uses of such a compound or mutein, for example, for the prevention and/or treatment of cancer, an auto-immune disease, or an infectious disease.

IC ICM A61K

CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 3, 63

IT **Polyoxyalkylenes, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, for extended shelf-life; muteins of human neutrophil gelatinase-associated lipocalin with affinity for CTLA-4 and their use for treatment of cancer, infectious, or (auto)immune diseases)

IT 50-18-0D, Cyclophosphamide, conjugates 51-21-8D, 5-Fluorouracil, conjugates 57-22-7D, Vincristine, conjugates 58-05-9D, Leucovorin, conjugates 58-85-5D, Biotin, conjugates 59-05-2D, Methotrexate, conjugates 362-07-2D, 2-Methoxyestradiol, conjugates 865-21-4D, Vinblastin, conjugates 4342-03-4D, Dacarbazine, conjugates 7440-57-5D, Gold, colloidal, conjugates 7689-03-4D, Camptothecine, conjugates 15663-27-1D, Cisplatin, conjugates 20585-97-1D, Curacin, conjugates 23214-92-8D, Doxorubicin, conjugates 25316-40-9D, Adriamycin, conjugates 33069-62-4D, Paclitaxel, conjugates 33419-42-0D, Etoposide, conjugates 41575-94-4D, Carboplatin, conjugates 53643-48-4D, Vindesine, conjugates 61825-94-3D, Oxaliplatin, conjugates 71486-22-1D, Vinorelbine, conjugates 79394-15-3D, Dolastatin 1, analogs, conjugates 113440-58-7D, Calicheamicin, conjugates 114977-28-5D, Taxotere, conjugates 117048-59-6D, Combretastatin A-4, conjugates 139504-50-0D, Maytansinoid DM 1, compds., conjugates **205304-86-5D**, Tubulysin A, compds., conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muteins of human neutrophil gelatinase-associated lipocalin with affinity for CTLA-4 and their use for treatment of cancer, infectious, or (auto)immune diseases)

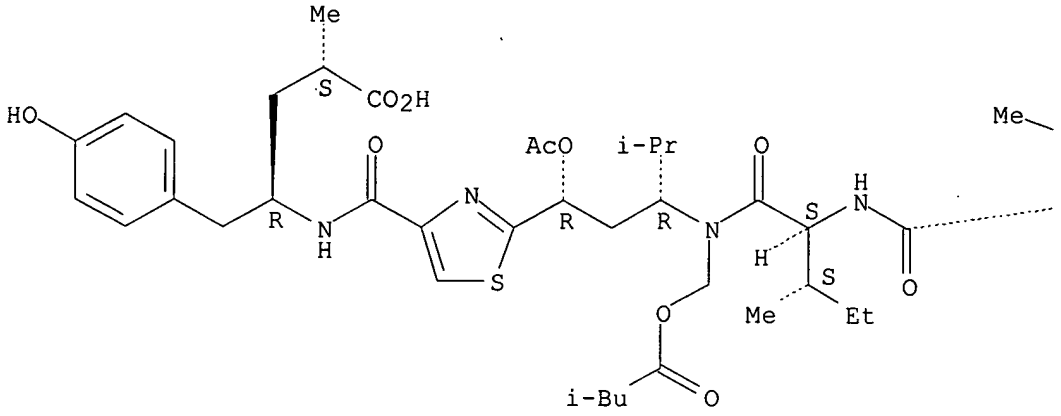
IT **205304-86-5D**, Tubulysin A, compds., conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muteins of human neutrophil gelatinase-associated lipocalin with affinity for CTLA-4 and their use for treatment of cancer, infectious, or (auto)immune diseases)

RN 205304-86-5 HCAPLUS

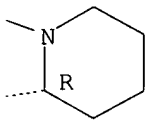
CN Benzenepentanoic acid, γ-[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-α-methyl-, (αS,γR)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L38 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:41504 HCAPLUS
DN 140:71010
TI Tubulysin conjugates with polymers or biomolecules, and use for the treatment of cancer
IN Doemling, Alexander; Weber, Lutz
PA Morphochem Aktiengellschaft fuer Kombinatorische Chemie, Germany
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004005326	A2	20040115	WO 2003-EP7415	20030709
	WO 2004005326	A3	20040219		

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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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	AU 2003253048	A1	20040123	AU 2003-253048	20030709
	EP 1521769	A2	20050413	EP 2003-762673	20030709
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PRAI	DE 2002-10230875	A	20020709		
	DE 2003-10305531	A	20030211		
	WO 2003-EP7415	W	20030709		

OS MARPAT 140:71010

AB The invention discloses tubulysin conjugates (e.g. of tubulysin A) with polymer or biomols. (e.g. antibodies) and the use thereof in the treatment of cancers.

IC ICM C07K0005-06
ICS A61K0047-48

CC 1-6 (Pharmacology)

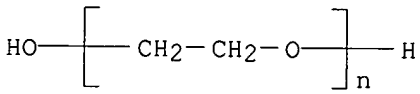
IT **Polyoxyalkylenes, biological studies**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tubulysin conjugates; tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

IT **25322-68-3D, Polyethylene glycol**, tubulysin conjugates **205304-86-5D**, Tubulysin A, conjugates with polymers or biomols.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

IT **25322-68-3D, Polyethylene glycol**, tubulysin conjugates **205304-86-5D**, Tubulysin A, conjugates with polymers or biomols.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI) (CA INDEX NAME)

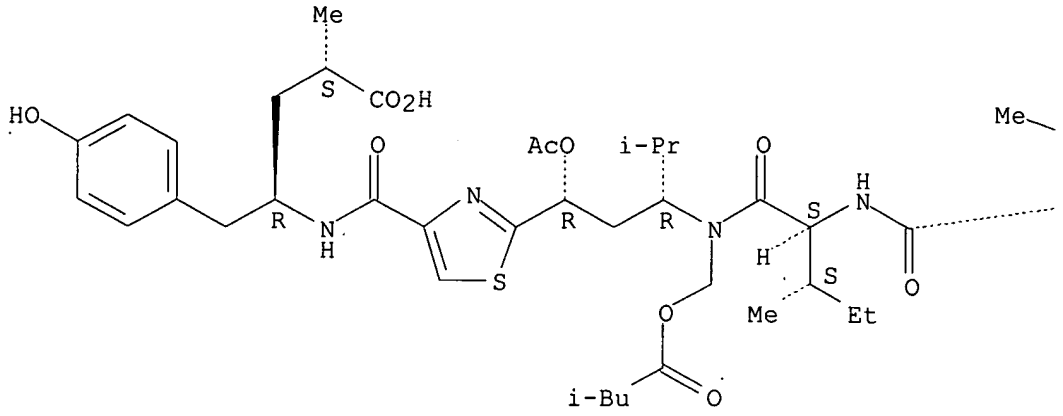


RN 205304-86-5 HCAPLUS

CN Benzenepentanoic acid, γ-[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-α-methyl-, (αS,γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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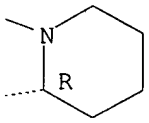

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FILE LAST UPDATED: 23 Jan 2007 (20070123/ED)
HIGHEST GRANTED PATENT NUMBER: US2007015693
HIGHEST APPLICATION PUBLICATION NUMBER: US2007016995
CA INDEXING IS CURRENT THROUGH 23 Jan 2007 (20070123/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Jan 2007 (20070118/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

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L47 ANSWER 1 OF 2 USPATFULL on STN
AN 2006:167882 USPATFULL
TI Bis(thio-hydrazide amides) for treatment of hyperplasia
IN Sherman, Matthew L., Newton, MA, UNITED STATES
Vaghefi, Farid, Burlington, MA, UNITED STATES
Chen, Lan Bo, Lexington, MA, UNITED STATES
PI US 2006142393 A1 20060629
AI US 2005-226929 A1 20050914 (11)

PRAI US 2004-610270P 20040916 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133, US
CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 2506
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and medical devices for treating a proliferative disorder in a subject, e.g., restenosis in a blood vessel that has been implanted with a stent, employ a bis(thio-hydrazide amide) represented by Structural Formula I or a pharmaceutically acceptable salt or solvate thereof. ##STR1## Y is a covalent bond or an optionally substituted straight chained hydrocarbyl group, or, Y, taken together with both >C=Z groups to which it is bonded, is an optionally substituted aromatic group.

R.sub.1-R.sub.4 are independently --H, an optionally substituted aliphatic group, an optionally substituted aryl group, or R.sub.1 and R.sub.3 taken together with the carbon and nitrogen atoms to which they are bonded, and/or R.sub.2 and R.sub.4 taken together with the carbon and nitrogen atoms to which they are bonded, form a non-aromatic heterocyclic ring optionally fused to an aromatic ring.

R.sub.7-R.sub.8 are independently --H, an optionally substituted aliphatic group, or an optionally substituted aryl group. Z is O or S.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . can be selected from the group consisting of polycarboxylic acids, cellulosic polymers, gelatin, polyvinylpyrrolidone, maleic anhydride polymers, polyamides, polyvinyl alcohols, **polyethylene oxides**, glycosaminoglycans, polysaccharides, polyesters, polyurethanes, silicones, polyorthoesters, polyanhydrides, polycarbonates, polypropylenes, polylactic acids, polyglycolic acids, polycaprolactones, polyhydroxybutyrate valerates, polyacrylamides, polyethers, and mixtures. . .
DETD . . . kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated hemoglobin **polyoxyethylene** conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate;. . .
IT 128-62-1, Narcosine 2068-78-2, Vincristine sulfate 2226-96-2, Tmpn 17313-52-9, Centaureidin 33927-09-2, Oncocidin a1 74588-78-6, D-64131 76129-16-3, IDN 5005 103614-76-2, Halichondrin b 108885-68-3, Taccalonolide a 110417-88-4, Dolastatin 10 115268-43-4, Fijianolide b 124784-31-2, Erbulozole 126268-81-3, Mivobulin isethionate 127943-53-7, Discodermolide 131727-01-0, Diazonamide a 134742-19-1, NSC-639829 143527-09-7 143842-96-0 149606-27-9, Auristatin pe 149715-96-8, Spongistatin 1 150624-44-5, Spongistatin 2 151852-31-2, Spongistatin 3 152044-53-6, Epothilone a 152044-54-7, Epothilone b 153698-80-7, Spongistatin 5 153745-94-9, Spongistatin 4 156294-36-9 156940-43-1 157207-90-4, Hemiasterlin 158080-65-0, Spongistatin 6 158681-42-6, Spongistatin 7 158734-18-0, Spongistatin 8 158734-19-1, Spongistatin 9 158809-58-6 158976-49-9 160237-10-5 160237-25-2 162084-71-1 162705-22-8, AC-7739 165659-77-8, KAR-2 170489-10-8, AM-97 172481-83-3 172837-41-1, Cemadotin hydrochloride 178927-85-0, Dz-3358 186256-67-7, Cryptophycin 52 186348-23-2 186692-73-9,

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(bis(thiohydrazide amides) for treatment of hyperplasia)

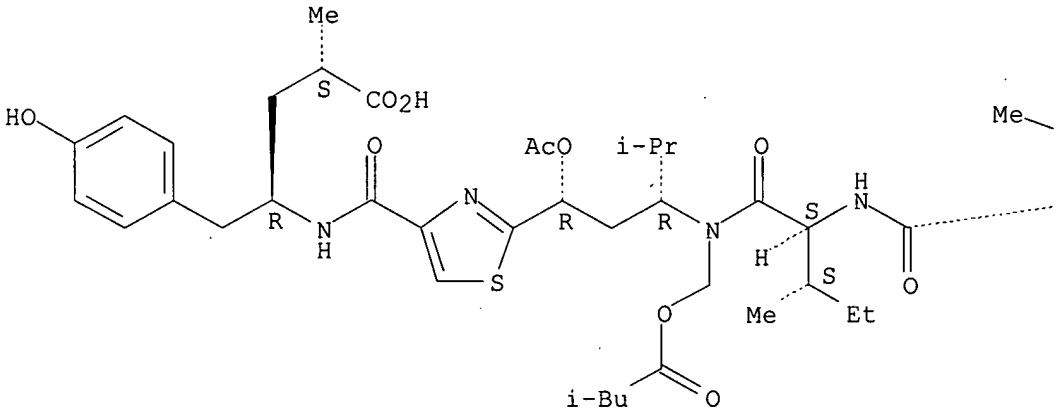
IT **205304-86-5**, Tubulysin a
(bis(thiohydrazide amides) for treatment of hyperplasia)

RN 205304-86-5 USPATFULL

CN Benzenepentanoic acid, γ-[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-α-methyl-, (αS,γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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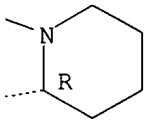


L47 ANSWER 2 OF 2 USPATFULL on STN
AN 2005:286476 USPATFULL
TI Tubulysin conjugates
IN Domling, Alexander, Munchen, GERMANY, FEDERAL REPUBLIC OF
Weber, Lutz, Germering, GERMANY, FEDERAL REPUBLIC OF
PA R & D Biopharmaceuticals GmbH (non-U.S. corporation)
PI US 2005249740 A1 20051110
AI US 2003-520791 A1 20030709 (10)
WO 2003-EP7415 20030709
20050108 PCT 371 date
PRAI DE 2002-10230875 20020709
DE 2003-10305531 20030211
DT Utility
FS APPLICATION
LREP EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA, 02205, US
CLMN Number of Claims: 8
ECL Exemplary Claim: 1-6
DRWN No Drawings
LN.CNT 415
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to novel tubulysin conjugates (e.g. of tubulysin A) and the use thereof in the treatment of cancer diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . 40,000; especially MW=25,000-100,000 Da, perferably 25,000-50,000 Da), polyethylenglycol dendrimers, polyacrylic acid, hydroxyethyl starch (HES), polylactic-glycolid, poly-D,L-lactic acid-p-dioxanonepolyethylene glycol block copolymer (PLA-DX-**PEG**), poly(ortho) ester, polyglutamate, polyaspartate, polymer from α-β-unsaturated monomers: (meth)acrylic acid, crotonic acid, maleic acid, maleic anhydride, fumaric acid, itaconic acid/anhydride,. . .
SUMM Further preferred the polymer is a **polyethyleneglycol** **PEG** (especially a **PEG** with a molecular weight of more than 30 kDa to 100 kDa, preferred of max. 50 kDa), which especially is. . .
DETD To a solution of 0.056 mmol Tubulysin A and 0.125 mmol **PEG** (6 kDa, 10 kDa, 20 kDa, 35 kDa and 40 kDa, resp.) in a miture of 3 ml acetonitrile and. . .
DETD The diamines of the **polyethyleneglycols** (6 kDa, 10 kDa, 20 kDa, 35 kDa bzw. 40 kDa) as well as their conjunction with Tubulysin A were. . .
DETD The **PEG** dicarbonic acids (6 kDa, 10 kDa, 20 kDa, 35 kDa bzw. 40 kDa) as well as their conjugation with Tubulysin. . .
CLM What is claimed is:
9. A compound of claim 7 wherein the polymer is a **polyethylene**

glycol.

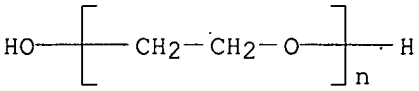
IT **Polyoxyalkylenes, biological studies**
(tubulysin conjugates; tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

IT **25322-68-3D**, Polyethylene glycol, tubulysin conjugates
205304-86-5D, Tubulysin A, conjugates with polymers or biomols.
(tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

IT **25322-68-3D**, Polyethylene glycol, tubulysin conjugates
205304-86-5D, Tubulysin A, conjugates with polymers or biomols.
(tubulysin conjugates with polymers or biomols., and use for treatment of cancer)

RN 25322-68-3 USPATFULL

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 205304-86-5 USPATFULL

CN Benzenepentanoic acid, γ-[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(3-methyl-1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-4-hydroxy-α-methyl-, (αS,γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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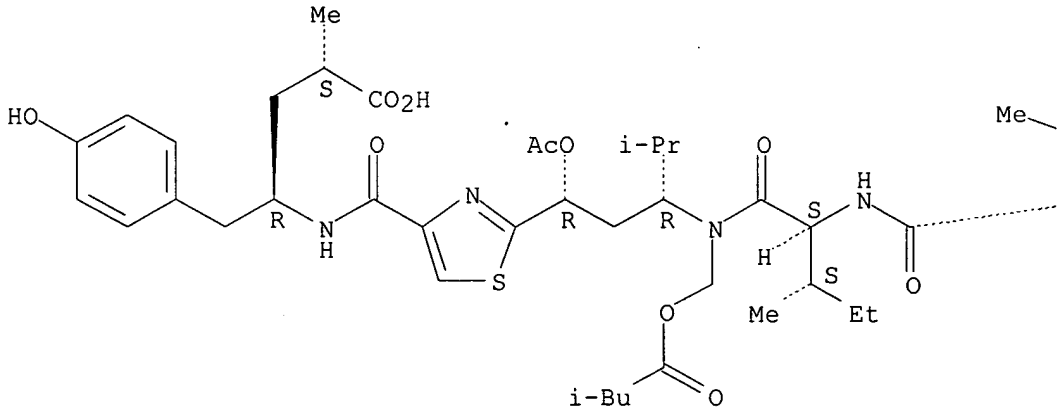

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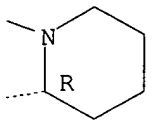


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L5           318 S E3-E15
                 E WEBER LUTZ/AU
L6           205 S E3-E9
                 E MORPHOCHEM/PA,CS
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L9           117 S L7,L8
L10            7 S L1-L9 AND TUBULYSIN?
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L24            0 S L23 AND C2H4O
L25           14 S L23 NOT L15
L26            1 S PEG/CN

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L29           1 S L1-L10 AND L28
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L33           0 S L27 AND (PEG OR POLYETHYLENEGLYCOL OR POLYETHYLENEOXIDE OR PO
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L36           0 S L27 AND (POLYOXY ETHYLENE OR POLY()(OXYETHYLENE OR OXY ETHYLE
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L44           0 S L39 AND (POLYOXY ETHYLENE OR POLY()(OXYETHYLENE OR OXY ETHYLE
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L47           2 S L40-L46

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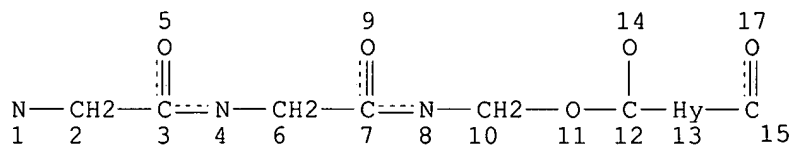


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FILE COVERS 1907 - 23 Jan 2007  VOL 146 ISS 5
FILE LAST UPDATED: 22 Jan 2007  (20070122/ED)

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 substance identification.

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L17  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
AN   2004:1060832  HCAPLUS
DN   142:43740
TI   Aptamer-toxin molecules and methods for using same
IN   Stanton, Martin; Kurz, Markus; Wilson, Charles
PA   USA
SO   U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 600,007.
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CODEN: USXXCO
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004249130	A1	20041209	US 2004-826077	20040415 <--
	US 2004022727	A1	20040205	US 2003-600007	20030618 <--
	AU 2004232848	A1	20041104	AU 2004-232848	20040421
	CA 2523260	A1	20041104	CA 2004-2523260	20040421
	WO 2004094614	A2	20041104	WO 2004-US12670	20040421
	WO 2004094614	A3	20060727		
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	EP 1620547	A2	20060201	EP 2004-760163	20040421
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	US 2005124565	A1	20050609	US 2004-873853	20040621 <--
	US 2005159351	A1	20050721	US 2004-980211	20041102 <--
	WO 2005116255	A2	20051208	WO 2005-US12797	20050415
	WO 2005116255	A3	20060413		
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PRAI	US 2002-390042P	P	20020618 <--		
	US 2003-600007	A2	20030618		
	US 2002-428102P	P	20021121 <--		
	US 2003-441357P	P	20030121		
	US 2003-463095P	P	20030415		
	US 2003-464179P	P	20030421		
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	US 2003-465053P	P	20030423		
	US 2003-465055P	P	20030423		
	US 2003-469628P	P	20030508		
	US 2003-474133P	P	20030529		
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	US 2003-486580P	P	20030711		
	US 2003-489810P	P	20030723		
	US 2003-491019P	P	20030729		
	US 2003-503596P	P	20030916		
	US 2003-512071P	P	20031017		
	US 2003-523935P	P	20031121		

	US 2003-718833	A	20031121
	US 2004-537045P	P	20040116
	US 2004-537201P	P	20040116
	US 2004-762915	A	20040121
	US 2004-826077	A	20040415
	US 2004-829504	A2	20040421
	WO 2004-US12670	W	20040421
	US 2004-873853	A2	20040621

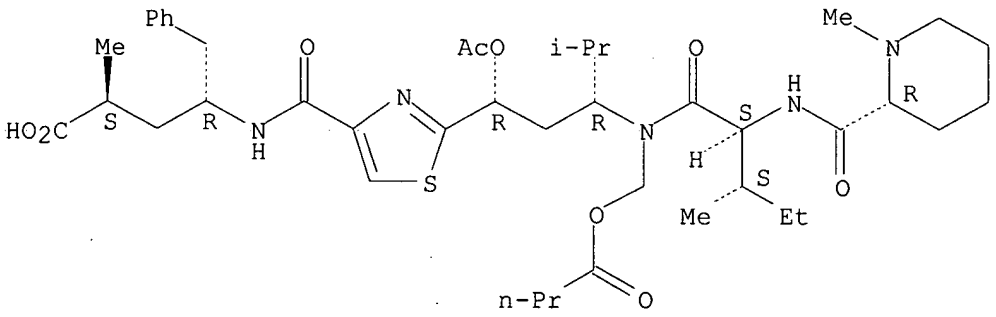
AB Materials and methods are provided to prepare therapeutic **conjugates** for the treatment of proliferative diseases. The therapeutic **conjugates** of the invention comprise a targeting moiety **conjugated** to a therapeutic moiety. The therapeutic moiety of the **conjugates** of the present invention have a cytotoxic effect and are useful in the treatment of proliferative diseases.

IT **309935-58-8D**, Tubulysine, derivs., aptamer **conjugates**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aptamer-toxin **conjugates** for targeted treatment of proliferative diseases)

RN 309935-58-8 HCAPLUS

CN Benzenepentanoic acid, γ-[[[2-[(1R,3R)-1-(acetyloxy)-4-methyl-3-[[(2S,3S)-3-methyl-2-[[[(2R)-1-methyl-2-piperidinyl]carbonyl]amino]-1-oxopentyl][(1-oxobutoxy)methyl]amino]pentyl]-4-thiazolyl]carbonyl]amino]-α-methyl-, (αS,γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:41504 HCAPLUS
DN 140:71010
TI **Tubulysin conjugates** with polymers or biomolecules, and use for the treatment of cancer
IN Doemling, Alexander; Weber, Lutz
PA Morphochem Aktiengellschaft fuer Kombinatorische Chemie, Germany
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004005326	A2	20040115	WO 2003-EP7415	20030709 <--
WO 2004005326	A3	20040219		

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PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10230875	A1	20040122	DE 2002-10230875	20020709	<--
DE 10305531	A1	20040819	DE 2003-10305531	20030211	
AU 2003253048	A1	20040123	AU 2003-253048	20030709	<--
EP 1521769	A2	20050413	EP 2003-762673	20030709	<--
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US 2005249740	A1	20051110	US 2005-520791	20050108	<--
PRAI DE 2002-10230875	A	20020709	<--		
DE 2003-10305531	A	20030211			
WO 2003-EP7415	W	20030709			

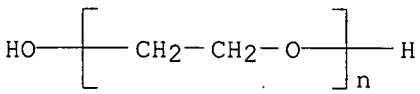
OS MARPAT 140:71010

AB The invention discloses **tubulysin conjugates** (e.g. of **tubulysin** A) with polymer or biomols. (e.g. antibodies) and the use thereof in the treatment of cancers.

IT **25322-68-3D, Polyethylene glycol, tubulysin conjugates**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tubulysin conjugates** with polymers or biomols., and use for treatment of cancer)

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI) (CA INDEX NAME)



L17 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:754431 HCAPLUS

DN 137:274074

TI Recombinant production of polyanionic polymers, and uses thereof as drug carriers for improvement of bioactivity and water-solubility

IN Leung, David W.; Bergman, Philip A.; Lofquist, Alan; Pietz, Gregory E.; Tompkins, Christopher K.; Waggoner, David W., Jr.

PA Cell Therapeutics Inc, USA

SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002077036	A2	20021003	WO 2002-US8614	20020321 <--
WO 2002077036	A3	20040129		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2002169125	A1	20021114	US 2002-101487	20020320 <--
	AU 2002252429	A1	20021008	AU 2002-252429	20020321 <--
	US 2005118136	A1	20050602	US 2004-939988	20040914 <--
PRAI	US 2001-277705P	P	20010321 <--		
	US 2002-101487	A3	20020320 <--		
	WO 2002-US8614	W	20020321 <--		

AB The invention provides a method for constructing a expression cassette that produce a polyanionic polymer that can be used as drug carriers to improve the bioactivity and water-solubility properties of a drug. The inventive method provides a monodispersed preparation of a recombinantly-produced polyanionic polymer that can be easily manipulated, such as lengthened. An active moiety may be chemical or recombinantly joined to a polyanionic polymer to increase its biol. half-life and/or solubility The instant invention also provides a method for targeting the delivery of a polyanionic polymer **conjugate** or fusion protein to a specific cell type or tissue.

IT Proteins
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(**conjugates**, with polyanionic polymer; recombinant production of polyanionic polymers, and uses thereof as drug carriers for improvement of bioactivity and water-solubility)

IT Antitumor agents
(epothilones, dolastatins, or **tubulysins** fused with polyanionic polymer; recombinant production of polyanionic polymers, and uses thereof as drug carriers for improvement of bioactivity and water-solubility)